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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,327	05/23/2006	David Alan Owen	CELL-0310	4658

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EXAMINER	
MABRY, JOHN	

ART UNIT	PAPER NUMBER
1625	

MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,327	OWEN ET AL.	
	Examiner	Art Unit	
	JOHN MABRY	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/06/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Foreign Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). The certified copy has been filed in this application, filed on December 8, 2005. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for salts, does not reasonably provide enablement for hydrates and solvates. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

"The claims are drawn to hydrates and solvates. But the numerous examples presented all failed to produce a hydrate or solvate. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ... no evidence that such compounds even exist." The same circumstance appears to be true here: there is no evidence that solvates of these compounds actually exist; if they did, they would have formed. Hence, applicants must show that solvates can be made, or limit the claims accordingly."

Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for amended compounds and pharmaceutical compositions of Formula I, does not reasonably provide enablement for the term "isomer". The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Solomons clearly describes that isomers are different compounds that have the same molecular formula (see pages 183-184). Considering the broadest reasonable interpretation of the meaning of the claimed term "isomers", the Applicant attempts to claim all possible structures of Formula 1 with different connectivity. According to the Specification, Applicant is clearly not enabled for all isomers of claimed Formula 1.

Claims 1-17 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for m being 1; n being 1; R1 being unsubstituted alkyl and cycloalkyl, phenylalkyl (where phenyl is optionally substituted with halogen), tetrahydropyranyl, piperidinyl (N alkyl or -CO2akyl substituted or unsubstituted), unsubstituted phenyl and Cy being phenyl optionally substituted with halo, alkyloxy, unsubstituted alkyl and haloalkyl; Ra and Rb being H, does not reasonably provide enablement for R1, Cy, R1/R2, Ra and Rb being enabled for the entire scope as claimed and all claimed "optional substituents".

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir.

1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims: Scope of the compounds. Owing to the range of many variables, millions of highly substituted hydroxamate sulfonamide compounds are embraced.

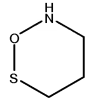
(2) The nature of the invention: The invention is a highly substituted hydroxamate sulfonamide compounds.

(3) Level of predictability in the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and chemical reactivity (which is affected by determinants such as substituent effects, steric effects, bonding, molecular geometry, etc) is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

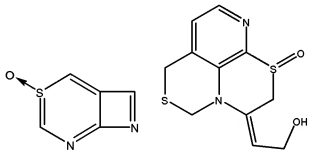
(4) Direction or Guidance: That provided is very limited. Applicant shows a general

synthesis of compounds of application's general formula 1. Pages 22-45 of the Specification describes starting materials and methods for synthesis of compounds wherein m being 1; n being 1; R1 being unsubstituted alkyl and cycloalkyl, phenylalkyl (where phenyl is optionally substituted with halogen), tetrahydropyranyl, piperidinyl (N alkyl or -CO2akyl substituted or unsubstituted), unsubstituted phenyl and Cy being phenyl optionally substituted with halo, alkyloxy, unsubstituted alkyl and haloalkyl; Ra and Rb being H, but does not reasonably provide enablement for R1, Cy, R1/R2, Ra and Rb being enabled for the entire scope as claimed. There is limited evidence in the Specification of the example compounds that only covers no or a small portion of the substituents claimed of formula. Thus, there is no specific direction or guidance regarding said compounds specifically mentioned in Scope.

For example, Applicant claims the term "heterocycloalkyl". Based upon Applicant's definition (see page 5, lines 20-23 of Specification), the following example can be devised. A preliminary search results, STN Structure database shows that these compounds do not exist. Additionally, these compounds cannot be purchase from Sigma-Aldrich (nor can reagents), in order synthesized compounds of claimed Formula 1. Applicant has not provided such guidance thus is not enabled to make compounds of the full scope as claimed.



Additionally, Applicant claims the term "heteroaryl". Based upon Applicant's definition (bottom of page 6 and top of page 7 of Specification), the following examples can be devised. Examiner has run a STN Structure Search and has reviewed the Aldrich Chemical Catalog for this molecule and potential precursors to make such molecule. Both of these inquiries failed to produce any results. This compound falls within the claimed scope of Applicant's invention and Applicant has not provided any sufficient guidance that would lead an artisan of ordinary skill to synthesize these molecules in particular and the full scope of the claimed "heteroaryls" of this invention.



The availability of the starting material that is needed to prepare the invention as claimed is at issue here...As per MPEP 2164.01 (b). A key issue that can arise when determining whether the specification is enabling is whether the starting materials or apparatus necessary to a make the invention are available. In the biotechnical area, this is often true when the product or process requires a particular strain of microorganism and when the microorganism is available only after extensive screening. The Court *in re Ghiron*, 442 F.2d 985, 991, 169 USPQ 723, 727 (CCPA 1971), made it clear that if the practice of a method requires a particular apparatus, the application must provide a sufficient disclosure of the apparatus if the apparatus is not readily

available. The same can be said if certain chemicals are required to make a compound or practice a chemical process. *In re Howarth*, 654 F.2d 103, 105, 210 USPQ 689, 691 (CCPA 1981).

It is not trivial to experimentally interchange any and all of the many substituents that exist. As generally described by F. Zaragoza Dörwald, most organic syntheses fail initially and chemical research is highly inefficient due to chemists spending most of their time "finding out what went wrong and why". Therefore, most syntheses of organic compounds are labor-intensive and demanding. Additionally, most final synthetic routes to desired organic molecules are usually very different from initially planned routes. A highly skilled chemist can agree that for many successful organic compounds made, many failures are encountered and experimental repetition is common. This also contributes to the burden and unpredictability of the syntheses of said compounds. (see "Side Reactions in Organic Synthesis: A Guide to Successful Synthesis Design" 2005 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.

(6) Working Examples: Applicant shows examples 1-26 (pages 22-45) but no working examples were shown wherein R1, Cy, R1/R2, Ra and Rb being enabled for the entire scope as claimed and all claimed "optional substituents" have been made or used of any kind.

(7) Skill of those in the art: The ordinary artisan is highly skilled, e.g. a masters or PhD

level chemist.

(8) The quantity of experimentation needed: Since there are very limited working examples as described above, the amount of experimentation is expected to be high and burdensome.

Due to the level of unpredictability in the art, the very limited guidance provide, and the lack of working examples, the Applicant has not provided sufficient guidance for the artisan to make the invention.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

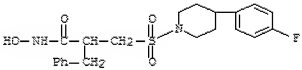
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

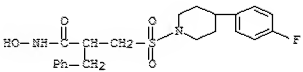
Claims 1-10, 13-15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Barlaam et al (WO 01/62751).

WO '751 discloses compounds and pharmaceutical compositions of Formula 1 where R4=H, R3=F, m=1, n=1, Ra and Rb=H, R2=H, R1=alkylphenyl (see Example 1, page 16).



Claims 1-10, 13-15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Martin et al (US 6,479,502).

US '502 discloses compounds and pharmaceutical compositions of Formula 1 where R4=H, R3=F, m=1, n=1, Ra and Rb=H, R2=H, R1=alkylphenyl (see Example 10, column 14).



Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

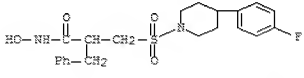
1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Martin et al (US 6,479,502).

The instant application claims compounds and pharmaceutical compositions of Formula 1 where (a) R3 is alkoxy or alkyl and (b) R1 and R2 together with the carbon to which they are attached for a cycloalkyl group.

Scope & Content of Prior Art MPEP 2141.01

US '502 discloses compounds and pharmaceutical compositions of Formula 1 where R4=H, R3=F, m=1, n=1, Ra and Rb=H, R2=H, R1=alkylphenyl (see Example 10, column 14).



Differences between Prior Art & the Claims MPEP 2141.02

US '502 teach that R10 of US '502 (R3 of instant application) can be:

(a) methoxy (see column 5, lines 45-46) and

(b) R1 and R2 (R3 of instant application) together with the carbon to which they are attached for a cycloalkyl group (see column 2, lines 39-67 where R2 of US '502 is represented by $R_2—(ALK)_m—(Q)_p—(ALK)_o—$ and m, p, o=0 and R3 is cycloalkyl.

Prima Facie Obviousness, Rational & Motivation MPEP 2142-2413

It would be obvious to one of ordinary skill in the art to take the disclosed species of US '502 and along with its teachings to achieve the compounds of the instant invention. US '502 clearly teaches that R3 of the instant application can be methoxy and that R1 and R2 (R3 of instant application) together with the carbon to which they are attached can form a cycloalkyl group. Additionally, the compounds of US '502 are used for the inhibition of metalloproteinase (see Abstract). This would provide further motivation for one of ordinary skill to use the species and genus teachings of US '502 to achieve the instant invention.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Mabry, PhD whose telephone number is (571) 270-1967. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's primary examiner can be reached at (571) 272-0684, or the Examiner's supervisor, Janet Andres, PhD, can be reached at (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/John Mabry/
Examiner
Art Unit 1625

/Janet L. Andres/
Supervisory Patent Examiner, Art Unit 1625